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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,997	04/09/2007	Stephen Gillies	ANTBH/P31763US	4525

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,997	GILLIES ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34,43-45 and 47-50* is/are pending in the application.

4a) Of the above claim(s) *47-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 May 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1 Claims 35-42, 46 and 51-52 are cancelled.

2. Claims 1-34, 43-45 and 47-50 are pending.

Election/Restrictions

3. Applicant's election without traverse of the invention of Group I, claims 1-34 and 43-45 in the reply filed on 29 May 2009 is acknowledged.

4. Claims 47-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

5. Claims 1-34 and 43-45 are under consideration.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 26 October 2007 has been fully considered by the examiner. A signed copy of the IDS is included with the instant Office Action.

Specification

7. The disclosure is objected to because of the following informalities:

a. The specification discloses that the BC1 antibody is a murine monoclonal antibody (e.g., see pp. 4-5; Carnemolla et al., J. Cell Biol. 109:1139-1148, 1989), however, the specification also discloses that the BC1 antibody is a human or humanised antibody (pg. 5). Further, the specification discloses a compound comprising a human BC1 heavy chain variable region of SEQ ID NO:1 and a human BC1 light chain variable region of SEQ ID NO:2 (see pg. 8-9). Thus, while one skilled in the art would recognize that a humanized BC1 antibody could be produced from the murine monoclonal BC1 antibody, the disclosure of a human BC1 antibody is inconsistent with the disclosure and prior art which defines that BC1 is a murine monoclonal antibody. The BC1 antibody cannot be a murine antibody and a human antibody.

Appropriate correction is required.

b. Applicant's cooperation is requested in reviewing and correcting any errors of which applicant may become aware in the specification.

Claim Objections

8. Claims 2, 9 and 33 are objected to because of the following informalities:

a. Claims 2 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

b. Claim 9 is objected to in the recitation "more at least 2-fold tighter…", which is grammatically incorrect. Consider revising the claim to recite "at least 2-fold tighter…".

c. Claim 33 is objected to in the recitation "SEQ ID 4", which should be corrected to "SEQ ID NO:4" for consistency and readability of the claim.

Appropriate correction is required.

Claim Rejections 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 11-13, 15, 19 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 15 is indefinite in the recitation "FAB-like molecules, such as...". The term "FAB-like molecules" is relative in nature, which renders the claims indefinite. The term "FAB-like molecules" is not defined by the claims; the specification does not provide a standard for

ascertaining the direction, requisite degree or endpoint, and one of ordinary skill in the art would not reasonably be apprised of the metes and bounds of the invention. Further, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

b. Claim 19 is indefinite for reciting "derived" because the exact meaning of the term is not clear. The term "derived" is not one, which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this term is the absence of an ascertainable meaning for said term. Since it is unclear the nature, extent and direction in which the Fc moiety is to be derivatized to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said term. In addition, since the term "derived" does not appear to be clearly defined in the specification, and the term can encompass Fc regions with amino acid substitutions, insertions, or deletions, chemically derivatized molecules, or even mimetics. In the absence of a single defined art recognized meaning for the term and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

c. Claims 11-13 and 30-33 are indefinite in the recitation "a polypeptide of SEQ ID NO…" as the exact meaning cannot be ascertained. SEQ ID Nos:1, 2, 4, 6 and 7 are each disclosed as single polypeptides, however, the recitation "a polypeptide of SEQ ID NO..." implies multiple polypeptides of each SEQ ID number, making it unclear what is contemplated by the phrase. Amending the claims to recite "the polypeptide of SEQ ID NO…" would provide clarity and overcome the instant rejection.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 5-6, 8-10 and 20 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line, which produces an antibody having the exact chemical identity of antibody BC1 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Fundamental immunology, William E. Paul, M.D. ed., 3rd ed., pg. 242, 1993. Therefore, it would require undue experimentation to reproduce the claimed antibody species, antibody BC1.

The specification lacks complete deposit information for the deposit of anti-oncofetal fibronectin antibody BC1. It is unclear whether antibodies possessing the identical properties of antibody BC1 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas

which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibody BC1, a suitable deposit is required for patent purposes, evidence of public availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of antibody BC1 has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of antibody BC1 is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

> (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:
> (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:
> (c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
> (d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. See MPEP 2406 and 37 CFR 1.804(b).

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

13. Claims 1-29, 34 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (see MPEP 2163).

The claims are drawn to a compound comprising or consisting of a monoclonal antibody having specificity for oncofetal fibronectin, or a fragment or variant thereof which retains the

binding specificity for oncofetal fibronectin of the parent monoclonal antibody and an effector portion comprising or consisting of IL-12, or a functional fragment or variant thereof, wherein the monoclonal antibody binds a region of oncofetal fibrocnectin other than the ED-B region. Thus, the scope of the claims includes a genus of antibody variants and IL-12 functional fragments or variants thereof and the genus is highly variant inclusive to numerous structural variants because a significant number of structural differences between genus members is permitted. The specification defines an IL-12 functional fragment or variant thereof to include fragments and variants capable of stimulating a Th1 immune response in a mammalian host, i.e., differentiation of Th1 cells from naive T cells (specification at pg. 9). The recitation of a "variant thereof" of a monoclonal antibody having specificity for oncofetal fibronectin and the recitation "functional fragment or variant thereof" of IL-12 does not convey a common structure or function and is not so defined in the specification. Although the specification teaches that antibody variants and IL-12 functional fragments and variants can be readily screened, the specification and the claim do not provide any guidance on the structure of the polypeptide and what changes can or can not be made. For example, Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79(6):1979-1983, March 1982) teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., *Eli Lilly*.

Further, it is not sufficient to define it solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CAFC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function" and the expression "an antibiotic penicillin"

fails to distinguish a particular penicillin molecule from others possessing the same activity and which therefore, fails to satisfy the written description requirement. Similarly, the function of retaining the binding specificity for oncofetal fibronectin does not distinguish a particular antibody "variant thereof" from others having the same activity or function and as such, fails to satisfy the written-description requirement. Additionally, the function of stimulating a Th1 immune response in a mammalian host does not distinguish a particular IL-12 "functional fragment or variant thereof" from others having the same activity or function and as such, fails to satisfy the written-description requirement. Applicant has not disclosed any relevant, identifying characteristics, such as structure or other physical and/or chemical properties, sufficient to show possession of the claimed genus of antibody variants and IL-12 fragments and variants that function equivalently. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Conception does not occur unless one has a mental picture of the structure of the molecule, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it.

Structural features that could distinguish a variant thereof of a monoclonal antibody that binds oncofetal fibronectin, and that could distinguish a functional fragment or variant thereof" of IL-12 in the genus from others in the protein class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure does not describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function of the binding oncofetal fibronectin and stimulating a Th1 immune response in a mammal host alone are insufficient to describe the genus of an antibody "variant thereof" and an IL-12 "functional fragment or variant thereof" that function equivalently. The recitations "variant thereof" and "functional fragment and variant thereof" does not convey a common structure nor a common function. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written

description for the highly variant genus of single function antibody variants ("variant thereof") and single function IL-12 functional fragments and variants thereof and one skilled in the art would not recognize that applicants had possession of the genus of claimed antibody variants which retain binding specificity for oncofetal fibronectin, nor possession of the claimed IL-12 functional fragments and variants thereof as instantly claimed.

Therefore, only a monoclonal antibody and fragments thereof (e.g., Fab, F(ab')2, Fv, dsFv, scFv) that bind oncofetal fibronectin and interleukin-12, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-7, 11-27, 34 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007) and Gillies et al [b] (US Patent 6,838,260 B2, priority to 12/8/1997).

The applied reference (Gillies et al [b]) has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Mariani et al teach monoclonal antibody BC1 that binds human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC-1 showed favorable tumor targeting *in vivo* (see entire document, particularly pp. 2485, 2487-2489). Mariani et al do not specifically teach BC1-IL-12 fusion proteins, humanized BC1-IL-12 or scFv-IL-12 (e.g., single-chain-IL-12) fusion proteins, or wherein the BC1 comprises the heavy chain variable region of SEQ ID NO:1 and the light chain variable region of SEQ ID NO:2, or wherein IL-12 is human, wherein the IL-12p35 domain is conjugated to the IL-12p40 domain by a disulfide bond or a composition comprising

the BC1-IL-12 fusion protein and a pharmaceutically acceptable carrier. These deficiencies are made up for in the teachings of Gillies et al [a] and Gillies et al [b].

Gillies et al [a] teach antitumor antibody-IL-12 fusion proteins comprising human p35 and p40 domains that induce active antitumor immune responses within the tumor microenvironment and provides an important alternative to systemic IL-12 administration or gene therapy for increasing its therapeutic index, wherein the antibody-IL-12 fusion proteins include whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12 (see entire document, particularly pp. 6195-6196 and 6200-6202).

Gillies et al [b] also teach antibody-IL-12 fusion proteins, including whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12 for cancer immunotherapy, wherein IL-12 comprises human p35 and p40 domains and may be linked by a disulfide bond (e.g., Fig. 1B) and Gillies et al teach the intravenous administration of the antibody-IL-12 fusion proteins in PBS buffer (e.g., pharmaceutically acceptable carrier), which unlike treatment with systemic IL-12, antibody-IL-12 fusion protein therapy can eradicate established metastatic colon carcinoma in a murine model (see entire document, particularly cols. 2-3, 5-6, Examples 5-8 and Figs. 1 and 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of Mariani et al and Gillies et al [a] and Gillies et al [b] because Mariani et al teach monoclonal antibody BC1 that binds human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC-1 showed favorable tumor targeting *in vivo* and Gillies et al [a] teach antitumor antibody-IL-12 fusion proteins comprising human p35 and p40 domains that induce active antitumor immune responses within the tumor microenvironment and provides an important alternative to systemic IL-12 administration or gene therapy for increasing its therapeutic index,

wherein the antibody-IL-12 fusion proteins include whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12 and Gillies et al [b] also teach antibody-IL-12 fusion proteins, including whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12 for cancer immunotherapy, wherein IL-12 comprises human p35 and p40 domains and may be linked by a disulfide bond (e.g., Fig. 1B) and Gillies et al [b] teach that unlike treatment with systemic IL-12, intravenous administration of antibody-IL-12 fusion proteins in PBS buffer (e.g., pharmaceutically acceptable carrier), can eradicate established metastatic colon carcinoma in a murine model. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated by the goal of increasing the therapeutic index of IL-12 by targeting IL-12 within the tumor microenvironment for inducing enhanced antitumor immune responses unlike those induced by systemic IL-12 and one of ordinary skill in the art would have been motivated to use the BC1 antibody or antigen-binding region thereof (e.g., Fab. F(ab')2, scFv) and humanized BC1 antibodies that target human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC1 showed favorable tumor targeting *in vivo*. Thus, there would have been advantages to targeting human IL-12 to the tumor microenvironment and the BC1 antibody or antigen binding fragments thereof target the human oncofetal fibronectin antigen, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of Mariani et al and Gillies et al [a] and Gillies et al [b]. Further, as evidenced by the specification at pp. 4-5, the BC1-IL-12 fusion proteins Mariani et al and Gillies et al [a] and Gillies et al [b] would necessarily bind to human oncofetal fibronectin via a site on repeat 7, outside the ED-B domain and would necessarily comprise the BC1 heavy chain variable region sequence of SEQ ID NO:1 and the BC1 light chain variable

region sequence of SEQ ID NO:2. Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

16. Claims 1, 5-6 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007) and Gillies et al [b] (US Patent 6,838,260 B2, priority to 12/8/1997) as applied to claims 1-7, 11-27, 34 and 43-45 above, and further in view of Schier et al (Journal of Molecular Biology, 263:551-567, 1996).

Mariani et al in view of Gillies et al [a] and Gillies et al [b] have been described supra. Mariani et al in view of Gillies et al [a] and Gillies et al [b] do not specifically teach wherein the BC1-IL-12 fusion proteins bind to oncofetal fibronectin at least 2-fold or at least 10-fold tighter than parental antibody BC1. This deficiency is made up for in the teachings of Schier et al.

Schier et al teach methods for producing a higher affinity antitumor antibody by restricting mutagenesis to the CDRs located at the center of the antibody combining site, which resulted in certain mutant antibodies having a 16-fold increase and a 1230-fold increase in affinity and according to Schier et al higher affinity antibodies with enhanced binding kinetics offer the possibility of significantly greater quantitative tumor retention (see entire document, particularly abstract, 553-554, 556 and Tables 2-4).

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced modified BC1-IL-12 fusion proteins having increased affinities for human oncofetal fibronectin for therapeutic benefit in cancer patients in view of Mariani et al and Gillies et al [a] and Gillies et al [b] and Schier et al because Schier et al teach a methods for producing a higher affinity antitumor antibody by

restricting mutagenesis to the CDRs located at the center of the antibody combining site, which resulted in certain mutant antibodies having a 16-fold increase and a 1230-fold increase in affinity and according to Schier et al higher affinity antibodies with enhanced binding kinetics offer the possibility of significantly greater quantitative tumor retention. Thus, there would have been an advantage to modifying the BC1 antigen-binding domain according to the teachings of Shier et al for producing high affinity BC1 antibodies having greater tumor retention for use in the BC1-IL-12 fusion proteins of Mariani et al and Gillies et al [a] and Gillies et al [b].

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

17. Claims 1 and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007) and Gillies et al [b] (US Patent 6,838,260 B2, priority to 12/8/1997) as applied to claims 1-7, 11-27, 34 and 43-45 above, and further in view of Gillies SD [c] (WO 02/79232 A2, published 10/10/2002).

Mariani et al in view of Gillies et al [a] and Gillies et al [b] have been described supra. Mariani et al in view of Gillies et al [a] and Gillies et al [b] do not specifically teach wherein the immunoglobulin heavy chain and the IL-12 (effector portion) are joined via a mutated linker sequence that comprises or consists of the amino acid sequence ATATPGAA. This deficiency is made up for in the teachings of Gillies [c].

Gillies [c] teaches the modification of amino acid residues at the junction of an antibody-cytokine fusion protein to reduce immunogenicity by elimination of MHC class II binding motifs, wherein the junction sequence LSLSPGKAP is changed to ATTAPGAAP that was incapable of binding to any human MHC class II with an affinity high enough to result in immunogenicity (see entire document, particularly pg. 16 and SEQ ID NO:18).

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-

IL-12) comprising the human IL-12p35 and IL-12p40 domains fused to the BC1 antibodies via the junction sequence ATATPGAAP for therapeutic benefit in cancer patients in view of Mariani et al and Gillies et al [a] and Gillies et al [b] and Gillies [c] because Gillies [c] teaches the modification of amino acid residues at the junction of an antibody-cytokine fusion protein to reduce immunogenicity by elimination of MHC class II binding motifs, wherein the junction sequence LSLSPGKAP is changed to ATTAPGAAP that was incapable of binding to any human MHC class II with an affinity high enough to result in immunogenicity. Thus, there would have been an advantage to using the junction peptide ATTAPGAAP of Gillies [c] to fuse the BC1 antibodies to the human IL-12p35 and IL-12p40 domains fused as taught by Mariani et al and Gillies et al [a] and Gillies et al [b].

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-7, 11-27, 34 and 43-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,226,998 in view of Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) and in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-8 of U.S. Patent No. 7,226,998 are drawn to a fusion comprising an immunoglobulin (Ig) moiety linked by a peptide bond to the p35 subunit of IL-12, the p35 subunit of IL-12 being linked to the p40 subunit of IL-12, wherein the Ig moiety comprises a single-chain Fv (scFv) antibody, the scFv antibody, wherein the Ig light chain variable region is N-terminal relative to the Ig heavy chain variable region, wherein the p35 subunit of IL-12 and the p40 subunit of IL-12 are linked by a disulfide bond, wherein the p35 subunit of IL-12 is linked to the amino terminus of the Ig moiety or Ig heavy chain, wherein the Ig moiety has antigen-binding specificity and a fusion protein comprising a single-chain Fv (scFv) antibody linked by a peptide bond to the p35 subunit of IL-12, the p35 subunit of IL- 12 being linked to the p40 subunit of IL-12, wherein the scFv antibody comprises an Ig heavy chain variable region linked by a linker sequence to an Ig light chain variable region. Claims 1-8 of U.S. Patent No. 7,226,998 do not specifically teach wherein the scFv antibody comprises the heavy and light chain variable regions of the BC1 antibody or wherein the antibody is the BC1 antibody, or a humanized BC1 antibody. These deficiencies are made up for in the teachings of Mariani et al and Gillies et al [a].

Mariani et al have been described supra.

Gillies et al [a] have been described supra.

The claims in the instant application are obvious variants of claims 1-8 of U.S. Patent No. 7,226,998 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-8 of U.S. Patent No. 7,226,998 and Mariani et al and Gillies et al [a].

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-8 of U.S. Patent No. 7,226,998 and Mariani et al and Gillies et al [a] because Mariani et al teach monoclonal antibody BC1 that binds human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC-1 showed favorable tumor targeting *in vivo* and Gillies et al [a] teach antitumor antibody-IL-12 fusion proteins comprising human p35 and p40 domains that induce active antitumor immune responses within the tumor microenvironment and provides an important alternative to systemic IL-12 administration or gene therapy for increasing its therapeutic index, wherein the antibody-IL-12 fusion proteins include whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to increase the therapeutic index of IL-12 by targeting IL-12 within the tumor microenvironment for inducing antitumor immune responses and one of ordinary skill in the art would have been motivated to target human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues using the BC1 antibody or antigen-binding region thereof (e.g., scFv), or humanized BC1 antibodies. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-8 of U.S. Patent No. 7,226,998 and Mariani et al and Gillies et al [a].

Claims 1-6, 11-15, 21-27 and 43-45 are directed to an invention not patentably distinct from claims 1-8 of commonly assigned U.S. Patent No. 7,226,998. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 7,226,998, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as

prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

20. Claims 1-7, 11-27, 34 and 43-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 in view of Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) and in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 are drawn to a heterodimeric fusion protein comprising a first and a second chimeric chain, said first chimeric chain comprising a portion of an Ig heavy chain linked by a peptide bond to a p35 subunit of IL-12 said second chimeric chain comprising a portion of an Ig heavy chain linked by a peptide bond to a p40 subunit of IL-12, said first and second chimeric chains being linked by a disulfide bond, and a fusion protein comprising a first chimeric Ig chain comprising a portion of an Ig heavy chain linked by a peptide bond to a p40 subunit of IL-12, said p40 subunit of IL-12 being linked to a p35 subunit of IL-12 and further comprising a second chimeric Ig chain comprising a portion of an Ig heavy chain linked by a peptide bond to a p40 subunit of IL-12, said p40 subunit of IL-12 being linked to a p35 subunit of IL-12 or vice versa, said first and second chimeric chains being linked by a disulfide bond. Claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 do not specifically teach wherein the antibody comprises the heavy and light chain variable regions of

the BC1 antibody or wherein the antibody is the BC1 antibody, or a humanized BC1 antibody. These deficiencies are made up for in the teachings of Mariani et al and Gillies et al [a].

Mariani et al have been described supra.

Gillies et al [a] have been described supra.

The claims in the instant application are obvious variants of claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 and Mariani et al and Gillies et al [a].

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 and Mariani et al and Gillies et al [a] because Mariani et al teach monoclonal antibody BC1 that binds human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC-1 showed favorable tumor targeting *in vivo* and Gillies et al [a] teach antitumor antibody-IL-12 fusion proteins comprising human p35 and p40 domains that induce active antitumor immune responses within the tumor microenvironment and provides an important alternative to systemic IL-12 administration or gene therapy for increasing its therapeutic index, wherein the antibody-IL-12 fusion proteins include whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to increase the therapeutic index of IL-12 by targeting IL-12 within the tumor microenvironment for inducing antitumor immune responses and one of ordinary skill in the art would have been motivated to target human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues using the BC1 antibody or antigen-binding region thereof (e.g., scFv), or humanized BC1

antibodies. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3 and 6-8 of U.S. Patent No. 6,838,260 B2 and Mariani et al and Gillies et al [a].

Claims 1-6, 11-15, 21-27 and 43-45 are directed to an invention not patentably distinct from claims 1-8 of commonly assigned U.S. Patent No. 6,838,260 B2. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,838,260 B2, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

21. Claims 1-7, 11-27, 34 and 43-45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 in view of Mariani et al (Cancer, 80(12 Suppl.):2484-2489, 1997, cited on PTO-892 mailed 4/27/09) and in view of Gillies et al [a] (The Journal of Immunology, 160(12):6195-6203, 1998, IDS reference filed 10/26/2007). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 are drawn to a fusion protein comprising a first polypeptide chain comprising an immunoglobulin region and a first subunit of IL-12 (p35 or p40) and a second polypeptide chain comprising a cytokine and a second subunit of IL-12 (p40 or p35), wherein the cytokine is a four-helix bundle protein, wherein the first and second polypeptides are covalently bonded by a disulfide bond. Claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 do not specifically teach wherein the antibody comprises the heavy and light chain variable regions of the BC1 antibody or wherein the antibody is the BC1 antibody, or a humanized BC1 antibody. These deficiencies are made up for in the teachings of Mariani et al and Gillies et al [a].

Mariani et al have been described supra.

Gillies et al [a] have been described supra.

The claims in the instant application are obvious variants of claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 and Mariani et al and Gillies et al [a].

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 and Mariani et al and Gillies et al [a] because Mariani et al teach monoclonal antibody BC1 that binds human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues and radiolabeled BC-1 showed favorable tumor targeting *in vivo* and Gillies et al [a] teach antitumor antibody-IL-12 fusion proteins comprising human p35 and p40 domains that induce active antitumor immune responses within the tumor microenvironment and provides an important alternative to systemic IL-12 administration or gene therapy for increasing its therapeutic index,

wherein the antibody-IL-12 fusion proteins include whole antibody-IL-12, humanized antibody-IL-12 and scFv-IL-12. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to increase the therapeutic index of IL-12 by targeting IL-12 within the tumor microenvironment for inducing antitumor immune responses and one of ordinary skill in the art would have been motivated to target human oncofetal fibronectin, which has extremely restricted distribution in normal adult tissues and is highly expressed in tumor tissues using the BC1 antibody or antigen-binding region thereof (e.g., scFv), or humanized BC1 antibodies. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced BC1-IL-12, humanized BC1-IL-12 and BC1 antigen-binding fragment-IL-12 fusion proteins (e.g., BC1scFv-IL-12) comprising the human IL-12p35 and IL-12p40 domains for therapeutic benefit in cancer patients in view of claims 1-3, 7 and 10 of U.S. Patent No. 6,617,135 B1 and Mariani et al and Gillies et al [a].

Claims 1-6, 11-15, 21-27 and 43-45 are directed to an invention not patentably distinct from claims 1-3, 7 and 10 of commonly assigned U.S. Patent No. 6,617,135 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,617,135 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

22. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643